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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/768,917	01/24/2001	Alain P. Vicari	SF0896K	5028

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EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/30/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/768,917	VICARI ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears n the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-24,26-36 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24,26-36 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment and response received on 5/15/03 has been entered. Claim 25 has been canceled. Claims 21-24, 26-36 and 39 are pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

Priority

The applicant has deleted the lines 5-6 of page 1 of the instant specification which claim a benefit of priority to EP 0 974 357 filed on 7/16/98. As noted in the previous office action, the instant application was filed more than twelve months after the filing date of the foreign application. Thus, priority to EP 0 974 357 has been denied. The effective priority date of the application is the actual filing date of instant application, 1/24/01.

Correction of Inventorship under 37 CFR 1.48(b)

In view of the papers filed on 5/15/03 under 37 CFR 1.48(b), the inventorship of this nonprovisional application has been changed by the deletion of Drake LaFace. The inventors of the instant invention as claimed are now Christophe Caux and Alain P. Vicari.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and USPTO PALM data to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 102

The rejection of claims 21-36 and 69 under 35 U.S.C. 102(a) as being anticipated by EP 0 974 357, 1/26/00, hereafter referred to as Caux et al., is withdrawn in view of applicant's change of inventorship under 37 CFR 1.48(b) which removed Drake LaFace as an instant inventor and further in view of the declarations under 37 C.F.R. 1.132 executed by Christophe Caux and Alain P. Vicari which states that Christophe Caux and Alain P. Vicari are the inventors of subject matter relating to MCP-4 and that the MCP-4 invention was disclosed to Serge Lebecque, Marie-Caroline Dieu, Betrice Vanbervliet, and Drake LaFace. Based on applicant's declarations and the change in inventorship, the EP 0 974 357 reference no longer qualifies as prior art under 35 U.S.C. 102(a) in regards to subject matter relating to MCP-4.

The rejection of claims 21-23, 35, 36, and 39 under 35 U.S.C. 102(b) as being anticipated by WO 98/14573, 4/9/98, hereafter referred to as Luster et al., is withdrawn in view of applicant's amendments to the claims.

Applicant's claim amendments have resulted in the following new grounds of rejection under 35 U.S.C. 102(b) and 35 U.S.C. 103(a).

Claims 21-24, 26-32, 35-36, and 69 are newly rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/46392 (9/16/99), hereafter referred to as Kwak et al. The applicant's claims as amended recite methods of enhancing an immune response in a mammal comprising administering MCP-4 in combination with an antigen. The applicant further claims said methods wherein the MCP-4 is administered in the form of a vector or a fusion protein, wherein the antigen is a tumor antigen, or viral antigen, or wherein the MCP-4 is administered intradermally or intramuscularly. The applicant also claims said methods wherein a non-methylated CpG "dendritic cell activating agent" is administered with the MCP-4 and antigen.

Kwak et al. teaches inducing immune responses effective to treat cancer or HIV infection by administering a fusion protein or a nucleic acid encoding a fusion protein which comprises either a tumor-antigen, such as Muc-1, or an HIV antigen and MCP-4 (Kwak et al., pages 4-6, 12-13, and page 105, claims 62-64). Kwak et al. further teaches the administration of said fusion protein in a form which allows for slow release, and the administration of the fusion protein by

intramuscular, topical or transdermal administration (Kwak, page 26, last paragraph, page 27, lines 22-25, and page 34, lines 15-19). Please note that while Kwak et al. does not specifically teach that the nucleic acid vectors encoding the MCP-4 fusion protein contain unmethylated CpGs, the presence of unmethylated CpGs in vector DNA prepared from bacteria is an inherent result of DNA replication in bacteria. Therefore, the plasmid vectors taught by Kwak inherently contains unmethylated CpGs. Thus, by teaching all the limitations of the claims as written, Kwak et al. anticipates the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-24, 26-36, and 69 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 974 357 A1 (7/16/98), hereafter referred to as Caux et al., in view of WO 98/14573 (4/9/98), hereafter referred to as Luster et al., and Dieu-Nosjean et al. (1999) J. Leuk. Biol. Vol. 66, 252-262. Please note, that while the EP 0 974 357 A1 document no longer qualifies as prior art under 102(a) regarding subject matter relating to MCP-4, this document does qualify as prior art in regards to the teachings contained therein relating to other chemokines such as MIP-3α.

The applicant's claims as amended recite methods of enhancing an immune response in a mammal comprising administering MCP-4 in combination with an antigen. The applicant further claims said methods wherein the MCP-4 is administered in the form of a vector or a fusion protein, wherein the antigen is a tumor antigen, or viral antigen, or wherein the MCP-4 is administered intradermally or intramuscularly. The applicant also claims said methods wherein a non-methylated CpG "dendritic cell activating agent" is administered with the MCP-4, or wherein the MCP-4 and antigen are co-administered with GM-CSF and IL4.

Caux et al. teaches methods of using chemokines in combination with antigens for directing the migration of antigen presenting cells, including dendritic cells, to lymphoid organs in vivo in order to increase immune responses (Caux et al., columns 4-6, and 18-19). In particular,

Caux et al. teaches the delivery of chemokines as a protein or a nucleic acid in combination with a viral, or tumor antigen (Caux et al., column 6, and columns 18-19, claims 11-14). Caux et al. further teaches the administration of non-methylated CpG as an "activating agent", the co-administration of GM-CSF and IL4, and the administration of the chemokine intradermally or intramuscularly (Caux et al., column 19, claims 17-20). Regarding the nature of chemokines useful for treating disease and inducing immune responses, Caux et al. teaches the use of chemokines, including MIP-3α, MIP-1α, and RANTES, which are capable of attracting and/or activating antigen presenting cells (Caux et al., columns 1-4).

While Caux et al. cannot be used as prior art for teaching MCP-4, Luster et al. supplements Caux et al. by teaching the administration of human MCP-4 in the form of a protein or a nucleic acid vector in order to stimulate immune responses in a mammal (Luster et al., pages 4-5, particularly page 5, lines 9-12). Luster et al. also teaches the construction and use of both bacterial and eukaryotic vectors encoding MCP-4 to express MCP-4 *in vivo*. (Luster et al., page 50). Luster et al. further teaches the MCP-4 is chemotactic for antigen presenting cells such as monocytes (Luster et al., pages 34-35). Dieu-Nosjean et al. further supplements Luster et al. by teaching that MCP-4 is capable of causing the activation and migration of dendritic cells (Dieu-Nosjean et al., page 255, Table 2). Thus, based on the known properties of MCP-4 in activating and attracting dendritic cells, and the teachings of Luster et al. that MCP-4 can be use to induce immune responses *in vivo* for the treatment of disease, it would have been *prima facie* obvious to the skilled artisan to use MCP-4 as the chemokine in the methods of inducing immune responses

comprising administering an antigen and a chemokine taught by Caux et al. Furthermore, based on the detailed teachings of Luster et al. for both protein and nucleic acid forms of human MCP-4, the skilled artisan would have had a reasonable expectation of success in co-administering an antigen and human MCP-4 in order to induce an immune response in a mammal.

Claim Rejections - 35 USC § 112

The rejection of claims 35 and 69 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicant's amendments to the claims.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER